SHORT REPORT

Behçet's syndrome: a report of 41 patients with emphasis on neurological manifestations

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Abstract

Forty one patients with the clinical diagnosis of Behçet's syndrome from two teaching hospitals in Kuwait were studied. There were 34 male and seven female patients. Age at presentation ranged from 14 to 48 years. Neurological manifestations were present in 24 patients. Eleven patients showed evidence of increased intracranial pressure, and 10 of these had radiologically confirmed dural sinus thrombosis. Five patients presented with a meningoencephalitic or meningomyelitic picture, three with a stroke-like picture, and three with primarily brain stem signs. One patient developed trigeminal neuritis, and five patients exhibited (along with other features) variable degrees of psychological manifestations. All patients with neurological involvement were treated with steroids, and some also had courses of other immunosuppressant drugs and colchicine. The disease took a relatively benign course, except those patients with meningoencephalitic and meningomyelitic presentation, one of whom died from the disease. Those treated early had a better prognosis. The incidence of dural sinus thrombosis in this series of patients is unusually high. In most patients, the course of the disease was more favourable than reported in the literature. This may be attributed to early and aggressive treatment.

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Behçet's syndrome is a chronic multisystem vasculitic syndrome. It was first recognised as a clinical entity by the Turkish dermatologist Hulusi Behçet in 1937, consisting of a triad of recurrent oral ulcerations, genital ulcerations, and relapsing inflammation of the eye.[1] Subsequently involvement of other organs was identified. The disease is well known to differ among different racial groups in presentation, predilection of system involved, and prognosis. We present our local experience in this disease, with emphasis on neurological manifestations.

Materials and methods

Forty one patients with the clinical diagnosis of Behçet's disease from two teaching hospitals were evaluated. All the patients fulfilled the International Study Group criteria for Behçet's disease.[2] All were assessed clinically and with baseline laboratory tests. Those patients with neurological manifestations were further studied in more detail. They were categorised according to the most prominent neurological features. The CSF was studied in 22 of the "neuro-Behçet syndrome" group and in 24 patients of the whole group.

Results

There were 34 male and seven female patients, with a male: female ratio of 4.8:1. Age of onset ranged from 14 to 48 years with a mean of 33.3 years. A majority of the patients (44%) presented between 20 and 30 years of age. There were 37 ethnic Arabs, two Indians, one Armenian, and one Iranian. Oral ulcers were the presenting feature in 30 patients, seven presented with multiple system involvement of an acute onset, and four patients presented with neurological complaints. All of the patients had oral ulcers. Genital ulcers were seen in 36 (78%), joint involvement in 22 (54%), eyes were affected in 17 patients (41%), recurrent venous thrombosis other than intracranial sinus thrombosis in nine (22%), gastrointestinal complications were seen in four (10%), and erythema nodosum in three (7%). Twenty four patients had neurological complications (59%). Major ophthalmological features included uveitis (anterior and posterior), synechiae, retinal vasculitis, conjunctivitis, and episcleritis.

NEUROLOGICAL MANIFESTATIONS

Neurological involvement was found in the 24 patients. Eleven had evidence of increased intracranial pressure presenting with a clinical picture similar to benign intracranial hypertension. Ten of these were proved to have dural sinus thrombosis either by MRI flow studies, MR angiography, or conventional angiogram. The remaining one patient was not evaluated radiologically. Three patients presented with a stroke-like picture, three had predominantly

Table 1 Group A: treatment and response

Patient No	*Treatment*								*Duration of neurological disease (y)*	*Duration of disease (y)*	*Response to treatment*
	Steroids	*Immuran*	*Colchicine*	*Clorambucil*	*Diamox*	*Warfarin*	*Cyclosporine*	*Others*			
3	+	+	+		+	+			3	3	Good
4	+		+		+				3	5	Good
7	+	+			+	+			3	6	Good
8	+		+		+	+			7	9	Good
10	+	+			+	+			9	12	Good
12	+	+	+		+				4	10	Good
17	+	+		+	+				?	?	Good
20	+				+				5	6	Good
21	+			+	+			Shunt	3	7	Optic atrophy
22	+				+				5	7	Good
24	+				+				5	8	Good

Table 2 Group B: clinical variety, treatment, and prognosis

Patient No	*Type of involvement*	*Treatment*					*Duration of neurological involvement (y)*	*Duration of disease (y)*	*Response to treatment*	*Beginning of treatment*
		Steroids	*Immuran*	*Colchicine*	*Clorambucil*	*Cyclosporine*				
2	Brain stem	+		+			3	3	Good	Early
5	Brain stem	+	+				4	14	Good	Early
9	Brain stem	+		+			6	6	Good	Early
11	Stroke	+	+				4	>6	Good	Late
13	Stroke	+	+				8	>5	Progressive	Late
14	Meningoencephalitis	+		+	+		8	8	Residual damage	Late
15	Meningoencephalitis	+			+		2	8	Residual damage	Late
16	Stroke	+	+				5	20	Severe residual disability	Late
18	Meningoencephalitis	+				+	7	7	Stable	Late
19	Meningomyelitis	+		+		+	3	7	Poor	Late
23	Meningoencephalitis	+		+	+		6	8	Died	Late

brain stem signs without disturbed consciousness (MRI showed demyelinating lesions in the brain stem), and five patients presented with acute meningoencephalitis or transverse myelitis occurring as single or recurrent attacks. One patient had a distinctive fascicular trigeminal neuritis involving the first and second branches of the trigeminal nerve and raised CSF protein (550 mg/l). Finally, one patient showed sociopathic behaviour and had recurrent headaches. His clinical examination and MRI study of the brain were normal. He refused CSF examination. Another four patients in the neurological group experienced mental or behavioural disturbances in addition to their neurological manifestations; one developed progressive dementia after repeated strokes, one had severe depression, one had acute psychosis, and one showed sociopathic behaviour. The mean duration of follow up was 4.6 years with a range of one to nine years. Out of the original 24 patients, 18 are still regularly followed up; five were lost after one to three years as they left the country during the Gulf War, and one patient died.

INVESTIGATIONS

High ESR and anaemia were found in 10 patients and these correlated well with the activity of the disease. A CSF study was performed in 22 patients. Increased cell counts were recorded in five patients and CSF protein was raised in seven Oligoclonal bands were positive in two

TREATMENT

Patients were followed up regularly at three to six month intervals. All patients with neurological involvement were treated with steroids, and some also had courses of other immunosuppressant drugs: colchicine, acetazolamide, and/or a thiazide diuretic, and four of them were given anticoagulant medication (tables 1 and 2). Duration of treatment varied among patients according to the type of neurological involvement and degree of response.

COURSE OF THE DISEASE DURING THE FOLLOW UP PERIOD

Of the 24 patients with neurological manifestations, 14 had an excellent response to treatment resulting in full remission or minimal residual disability. This included 10 out of the 11 patients with dural sinus thrombosis. Three patients had an unfavourable course: one had repeated strokes and subsequently developed progressive dementia, another had a transverse myelitis and was left with dense paraplegia, and a third had sagittal sinus thrombosis and developed optic atrophy and blindness. Out of the five patients who were lost to further follow up after one to three years, two had had meningoencephalitis or transverse myelitis. One patient with multiple strokes who had residual disability experienced no further cerebrovascular attacks after the beginning of treatment during the three years of his follow up. The remaining two were lost to follow up after one year; one had trigeminal neuritis, and the other showed sociopathic behaviour and had recurrent headaches.One of our patients died from the disease; this was a patient with severe fulminating parenchymatous CNS involvement manifested as recurrent attacks of meningoencephalitis. One patient with meningomyelitis has residual paraparesis, but has had no further episodes after having started treatment (eight years of follow up). All the other patients are still being followed up and are in a stable condition. Only five out of the 41

patients in our series had both neurological and ophthalmological complications. All the patients had minor ophthalmic complaints, but there were no particular neurological features related to the involvement of the eyes; nor was there any effect on the prognosis.

Discussion

Our patients have an age incidence and sex distribution comparable with that of the international experience.[3] In our series, however, there were fewer cases with erythema nodosum and a larger proportion of those with neurological manifestations. From a prognostic point of view, we could identify two main groups of patients (we exclude the two patients who were only followed up for a period of about one year). Group A (table 1) (11 patients) are those who presented with increased intracranial pressure, and they comprised 46% of the patients. They all had a benign disease except for one. Group B (table 2) (11 patients) are those who presented with parenchymatous or meningial involvement and generally had a poorer, although variable outcome. Two factors were found to be relevant for prognosis in these patients: (1) The site of the lesion and structure involved. Those with brain stem disease were better off than those with strokes, meningoencephalitis, or meningomyelitis; (2) The time interval between the onset of the neurological symptoms and the beginning of active treatment. Those who were diagnosed and treated early and vigorously had a far better outcome than the ones in whom diagnosis and treatment were delayed. However, even among those with appreciable residual disability a halt in the disease process was achieved once the treatment was instituted. Difference in medication regimens seemed to have little or no impact on the final outcome. The overall prognosis was excellent in 58% of patients, with just a single case of fatal outcome; this is significantly better compared to the 49% mortality in previous literature.[3] The reported frequency of CNS involvement in Behçet's disease is around 15–25% in most studies, with a range of 2.9% in Taiwan to 44% in Saudi Arabia.[3–5] We have noticed that most patient series with lower incidence of "neuro-Behçet syndrome" were reported by ophthalmologists,[4 6] and this either reflects a truly low rate of neurological manifestations among "ophthalmic-Behçet syndrome" patients (as was noticed in our cases) or merely underdiagnosing of cases with relatively mild neurological involvement. On the other hand, as expected, reports of higher percentages of neurological manifestations mainly came from internists and neurologists.[5 7 8] More than 50% of our 41 patients had neurological manifestations. A rather comparable proportion was found in Saudi Arabia, which has a population structure similar to that in Kuwait.[5] Whether these high ratios reflect a higher rate of referral of such patients to our hospitals or a true increased predisposition of population to neurological complications in this part of the world remains debatable. Another point of interest in our series of patients is that we had a larger proportion of patients with dural sinus thrombosis and benign intracranial hypertension-like presentation. They comprised 46% of our "neuro-Behçet syndrome" patients, compared with 33% in France,[8] 26% in Morocco,[9] 21.1% in Saudi Arabia,[5] 15.3% In Italy,[10] and none in Egypt.[7] This pattern of presentation may have contributed to the better prognosis noted in our series, as exactly these patients had the best response to treatment. We suggest, therefore, that oral and genital ulcers should be sought in every patient presenting with a benign intracranial hypertension-like picture.

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